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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/524,193	02/11/2005	Nobutaka Nakashima	081356-0232	4133
22428 7590 04/23/2008 FOLEY AND LARDNER LLP SUITE 500 3000 K STREET NW WASHINGTON, DC 20007				
EXAMINER				
POPA, ILEANA				
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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

### Office Action Summary

**Application No.**

10/524,193

**Applicant(s)**

NAKASHIMA ET AL.

**Examiner**

ILEANA POPA

**Art Unit**

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 28 January 2008.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 29 and 31 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 29 and 31 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-8508)  
Paper No(s)/Mail Date \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: \_\_\_\_\_

**DETAILED ACTION**

1. Claims 1-28, 30, and 32-42 have been cancelled. Claims 29 and 31 have been amended.

Claims 29 and 31 are pending and under examination.

2. The objection to the oath/declaration is withdrawn because Applicant submitted a new oath or declaration in compliance with 37 CFR 1.497(a) on 10/30/2007.

All objections/rejections pertaining to claims 1-17, 19-23, 26-28, and 30 are moot because Applicant cancelled the claims in the response filed on 01/28/2008.

The objection to claims 29 and 31 for depending from multiple dependent claims while being themselves multiple dependent is withdrawn in response to Applicant's amendments to the claims filed on 01/28/2008. It is noted that, due their improper dependent form, claims 29 and 31 were not treated on their merits (see the non-final Office action of 05/31/2007). In view of Applicant's amendments to the claims filed on 01/28/2008, claims 29 and 31 are presently examined as set forth below.

***Priority***

3. Acknowledgment is made of Applicant's submission of an English translation of the foreign priority document on 10/30/2007.

***Claim Rejections - 35 USC § 103***

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4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

5. Claims 29 and 31 are rejected under 35 U.S.C. 103(a) as being unpatentable over De Mot et al. (Microbiology, 1997, 143: 3137-3147, Applicant's IDS), in view of each Takano et al. (Gene, 1995, 166: 133-137, Applicant's IDS), Whyte et al. (Appl Environ Microbiol, 1998, 64: 2578-2584, of record), and Chiu et al. (J Biol Chem, 1999, 274: 20578-20586, of record).

De Mot et al. teach an expression vector for *R. erythropolis* (i.e., the vector comprises a DNA sequence essential to autonomous replication in *R. erythropolis*) (claim 29) and an *R. erythropolis* transformant comprising the above expression vector (claim 31) (Abstract, p. 3137, columns 1 and 2, p. 3138, columns 1 and 2). De Mot et al. do not teach their expression vector as having (i) an expression cassette comprising the *tipA* gene promoter, a multicloning site for the insertion of a foreign gene and a transcription termination sequence, (ii) an inducer cassette comprising a second promoter sequence and the *tipA* gene, and (iii) a thiostrepton resistance gene (claim 29). Takano et al. teach an inducible expression vector having a cassette comprising the *tipA* gene promoter, a multicloning site for the insertion of a foreign gene and a transcription termination sequence, wherein the inducible expression vector also contains the thiostrepton resistance gene (claim 29) (Abstract, p. 133, column 2, p. 134, column 1). Takano et al. also teach that their vector can be used for induced

expression of proteins when the cells are grown at the suitable temperature (p. 133, column 2). It would have been obvious to one of skill in the art, at the time the invention was made, to modify the expression vector of De Mot et al. by introducing the tipA promoter / thiostrepton inducible system of Takano et al. together with the thiostrepton resistance gene to control the expression of toxic genes, with a reasonable expectation of success. The motivation to use the tipA promoter / thiostrepton inducible system is provided by Takano et al., who teach that tipA promoter / thiostrepton system is a widely used and very efficient in controlling gene expression (p. 133, column 2). The motivation to use the thiostrepton resistance gene is also provided by Takano et al., who teach the need to provide resistance to thiostrepton upon induction (p. 134, column 1, first full paragraph). One of skill in the art would have been expected to have a reasonable expectation of success in making and using such an expression vector because the art teaches that such expression vectors can be successfully made and used. With respect to the limitation of the foreign gene being multiplied under low-temperature conditions (claim 29), this is an inherent property of *Rhodococcus* cells, which can be grown within a large temperature range from 0 °C to 35 °C (see for example Whyte et al., Abstract, p. 2579, column 1, third full paragraph, p. 2580, column 1). With respect to the limitation of the vector comprising a multicloning site (claim 26), this is an inherent property of any expression vector; all expression vectors have a multicloning site. With respect to the limitation of an additional inducer cassette comprising a promoter driving the expression of the *TipA* gene (claim 29), the vector of De Mot et al. and Takano et al. must necessarily contain this because, in the absence of

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*TipA* gene product, the thiostrepton / *tipA* promoter inducible system does not work (see Chiu et al., p. 20580, column 2, first full paragraph; Takano et al., p. 137, column 1, last paragraph). With respect to the specific vector pTIP-LNH1 set forth by SEQ ID NO: 110 recited in the instant claim 29, it is noted that there is no evidence on the record that the vector backbone results in a construct exhibiting an unexpected property. The essential components (i.e., the expression cassette comprising the *tipA* gene promoter, a multicloning site for the insertion of a foreign gene and a transcription termination sequence, the inducer cassette, the DNA region essential for the autonomous replication in *R. erythropolis*, and the thiostrepton resistance gene) and a vector comprising all these essential elements are taught by the combined art above. The difference between the claimed vector and the vector taught by De Mot et al., Takano et al., Whyte et al., and Chiu et al. is the vector backbone. The backbone is not significant if it does not provide a novel feature.

Thus, the claimed invention was *prima facie* obvious at the time the invention was made.

### ***Conclusion***

6. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ILEANA POPA whose telephone number is (571)272-5546. The examiner can normally be reached on 9:00 am-5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Ileana Popa, PhD

/Joseph T. Woitach/

Supervisory Patent Examiner, Art Unit 1633